not been demonstrated.

Substances (or groups of substances) that are considered to cause endocrine disruption are reported in the interim report (July, 1997) by "Exogenous Endocrine Disrupting Chemical Task Force" of Environment Agency. However, it is considered that the types of such substances would be further increased in the course of research and study in the future.

Known methods for determining endocrine disruptors are classified into two groups, i.e., in vitro methods and in vivo methods. Examples of the methods in the former group include a method in which a binding activity to estrogen receptor or androgen receptor is measured, and a method in which an activity of inhibiting a hormone synthesis enzyme system is measured. Examples of the methods in the latter group include a method in which production of various hormones and abnormal tissue formation in rats at different postnatal days are measured, a method in which abnormal metamorphosis in a frog is measured, and a method in which abnormal maturation in a fish is measured (Analytical Chemistry, 70(15):528A-532A (1998)).

However, it has not been clearly demonstrated to date whether or not the substances that are suspected to be endocrine disruptors with attention actually cause

endocrine disruption. Furthermore, if they cause endocrine disruption, the mechanism through which they influence as well as the amount and the length of the period of intake that might be risky have not been clearly demonstrated.

For example, the current binding test to a hormone receptor is necessary and important as a primary screening. However, the results obtained by this method do not guarantee the identity as an endocrine disruptor. Specifically, estradiol (a naturally occurring female hormone), diethylstilbestrol (a synthetic female hormone), isoflavone (a component contained in pulses which is harmless to humans) and bisphenol-A (a substance suspected to be an endocrine disruptor) bind to estrogen receptor, although the EC_{50} values for these substances are different each other. Thus, the degree of endocrine disrupting activity of each substance cannot be determined according to this assay method. Similarly, the activity cannot be determined according to any of the conventional methods including an assay system in which a yeast or a cultured cell is used, and a system in which uterine of a mouse is weighed.

In other words, the current methods in which a binding activity to a hormone receptor or an activity of inhibiting hormone synthesis enzyme system is measured in vitro meet a necessary condition as a method for measuring

an endocrine disruptor. However, they never meet a sufficient condition. Furthermore, methods in which influences on the growth or morphogenesis of a rat, a frog, a fish or the like are determined in vivo are less sensitive and complicated, and require a long period of time for operating a large number of samples.

In addition, although the conventional analysis methods as described above may be used to analyze the relationship between a potential endocrine disruptor and a receptor, they cannot be used to analyze the downstream signal transduction system.

As described above, it is necessary for solving problems of environmental hormones to identify endocrine disruptors and to determine the influences by the substances on the endocrine systems. Thus, methods for analyzing which signal transduction pathway is influenced by an endocrine disruptor and which substance causes endocrine disruption have been desired.

Objects of Invention

The main object of the present invention is to provide (1) a method for detecting a gene that is influenced by an endocrine disruptor; (2) a method for detecting a gene that is influenced by an endocrine disruptor which comprises measuring the expression of the